Early pseudoaneurysm degeneration in biologic extracellular matrix patch for carotid repair

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A newly-approved carotid patch, derived from porcine small intestinal submucosa (SIS), is thought to allow functional tissue regeneration by acting as a biologic scaffold of extracellular matrix. We report three cases of asymptomatic pseudoaneurysm after SIS patch closure. At exploration there were intact suture lines, no growth from cultures, and central patch herniation. Histopathologic examination showed postendarterectomy neointima in the artery and disorganized collagen in the pseudoaneurysm. SIS patch remnants adjacent to macrophage infiltration and neovascularization indicated ongoing processes of degradation and synthesis. Imbalances between degradation and host tissue synthesis are problems that may unpredictably affect SIS patch integrity. (J Vasc Surg 2014;59:1116-8.)

Patching of carotid endarterectomy (CEA) is a standard technique associated with improved short- and long-term outcomes.[1] Commonly used prosthetic patches include woven polyester, polytetrafluoroethylene, and glutaraldehyde cross-linked bovine pericardium, which heal as foreign body. A newly-approved patch derived from porcine small intestinal submucosa (SIS) (CorMatrix extracellular matrix [ECM] for carotid repair; CorMatrix Cardiovascular, Inc, Roswell, Ga) is thought to allow functional tissue regeneration by acting as a biologic scaffold of extracellular matrix.[2,3] We report development of three pseudoaneurysms within 6 months of CorMatrix ECM (CorMatrix Cardiovascular, Inc) carotid patch implantation.

CASE REPORTS

Case 1. A 75-year-old male with severe internal carotid stenosis and completed minor stroke underwent CEA and arteriotomy closure with SIS patch. Completion ultrasound was normal. Four months postoperatively a pulsatile neck mass was identified. Carotid ultrasonography and computed tomographic angiography (CTA) revealed dilation at the endarterectomy site measuring 2 cm in diameter and 3.5 cm in length. Exploration of the carotid bifurcation easily identified the suture line and the SIS patch healed to the artery. Centrally, the patch had a 1- × 2-cm defect filled with laminated mural thrombus. The SIS was excised, and the artery repaired with groin saphenous vein patch (SVP). Three months postoperatively, the patient was doing well with no neck masses and no neurologic deficit.

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Author conflict of interest: none.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214/$36.00

http://dx.doi.org/10.1016/j.jvs.2013.05.012

Case 2. A 63-year-old asymptomatic male presented with a chronically occluded left internal carotid artery and a critical right internal carotid stenosis. He underwent an elective right CEA and SIS patch closure. Completion ultrasound was unremarkable. Six months postoperatively a carotid duplex and CTA showed the carotid bulb with dimensions of 2.47 × 2.27 × 3.37 cm. The patient underwent exploration of his bifurcation with findings of intact suture line and a 2-cm central pseudoaneurysm. The SIS was excised, and the artery was closed with groin SVP. As of the 2-month follow-up, the patient is doing well.

Case 3. A 73-year-old woman presented with an asymptomatic 95% internal carotid stenosis and underwent an elective CEA with SIS patch closure. Completion ultrasound was normal, and she was discharged the next day. Four months postoperatively, a pulsatile right neck mass was identified. Duplex scan and CTA showed focal 1.4-cm dilation of the distal right common carotid. The patient underwent exploration. A 3-cm pseudoaneurysm originating from the center of the SIS was identified (Fig 1). The patch was excised, and the arterial defect closed with groin SVP. She is doing well after a 3-month follow-up visit.

Microbiologic and histologic examination. The excised patches had multiple cultures taken, which returned negative for aerobic and anaerobic bacterial growth. Histopathology showed fibromuscular tissue consistent with carotid artery and areas of chronic inflammation and fibrosis, consistent with pseudoaneurysm (Fig 2). The patches are recognized as orderly collagen bundles without cellularity. The patch-artery interface shows luminal matrix deposition in the form of disorganized collagen with marked cellularity. In the area of the pseudoaneurysm, the degraded patch is associated with macrophages and neovascularization (Fig 3) and surrounded by unorganized collagen with relatively few resident fibroblasts.

DISCUSSION

We implanted 37 CorMatrix ECM (CorMatrix Cardiovascular, Inc) patches in the carotid position and observed nearly a 10% incidence of pseudoaneurysm formation. This series of unusual complications prompted examination of published clinical results with SIS in the carotid position and consideration of Food and Drug Administration

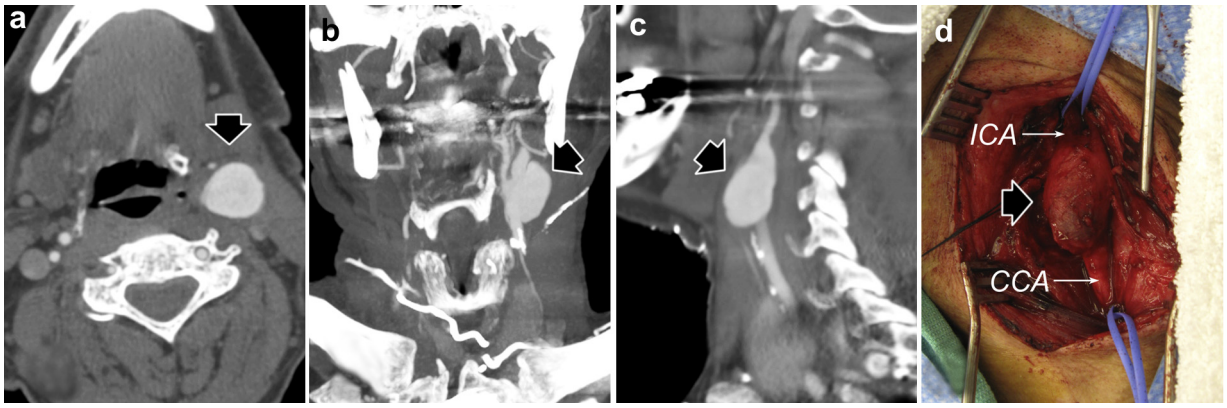

Fig 1. Carotid patch pseudoaneurysm. **a,** Axial computed tomography (CT) image. **b,** Coronal CT image demonstrating lobular superior extension (*arrow*). **c,** Sagittal CT image. **d,** Operative dissection from same patient showing common (*CCA*) and internal carotid (*ICA*) arteries with large small intestinal submucosa (SIS) patch pseudoaneurysm.

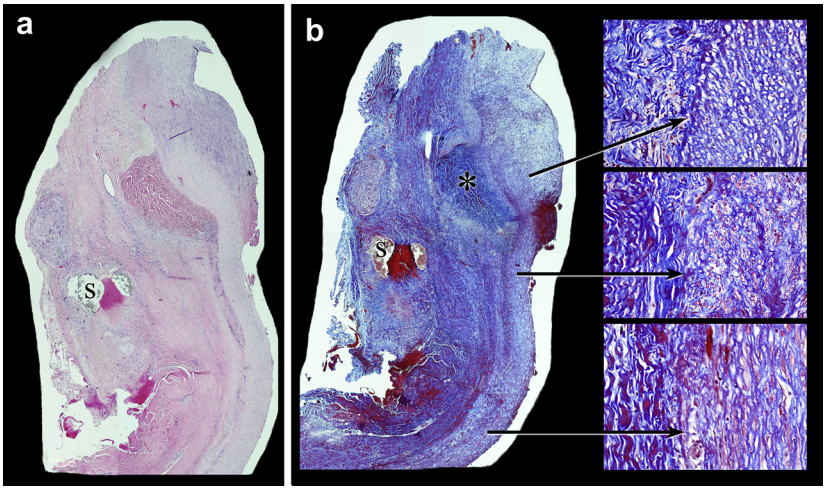

Fig 2. Excised patch and adjacent carotid artery. **a,** Patch pseudoaneurysm (*superior aspect*) and normal post-endarterectomy arterial architecture (*inferior aspect*) — hematoxylin and eosin stain. **b,** Masson Trichrome stain (low and high powers) delineates collagen fibers as basophilic. Inferior aspect shows well-organized collagen fibers of neointima luminal to normal smooth muscle. *Middle aspect* demonstrates acellular collagen of small intestinal submucosa (SIS) patch (*) and less organized transmural collagen fibers. *Superior aspect* shows disorganized collagen fibers of patch pseudoaneurysm. *S,* Suture.

approval processes for newly devised products in this category.

In humans, SIS has been used to repair both vascular and cardiac defects. In cardiac surgery, it is frequently employed for closure of the pericardium and less commonly for repair of intracardiac[4] or local aortic defects.[5] Long-term outcomes for intracardiac and thoracic aortic reconstructions are unknown. In the carotid artery, a single study has examined SIS. McCready et al[6] implanted four-ply SIS (Surgisis; Cook Biotech, Inc, West Lafayette, Ind) in 76 patients undergoing patch angioplasty after CEA as part of an institutional review board-approved investigational trial under the auspices of Cook Biotech, Inc. Seven asymptomatic pseudoaneurysms were discovered, and the trial was immediately discontinued. All degenerated SIS patches were implanted over an 8-week period, identified less than 10 weeks after endarterectomy, and came from two specific material lots. Treatment (interposition vein grafting in two, covered stents without cerebral protection in four and observation in one) resulted in three strokes. Histopathologic examination of one explanted patch revealed circumferentially arranged smooth muscle cells and absent endothelium. Mechanical testing of the two material lots demonstrated thinner and more variable physical characteristics compared with controls. These workers suggested a minimal SIS patch thickness of 3 mm was important to prevent degeneration. Although CorMatrix ECM (CorMatrix Cardiovascular, Inc) patches were commercially available and six-ply, our findings of pseudoaneurysm formation less than 6 months

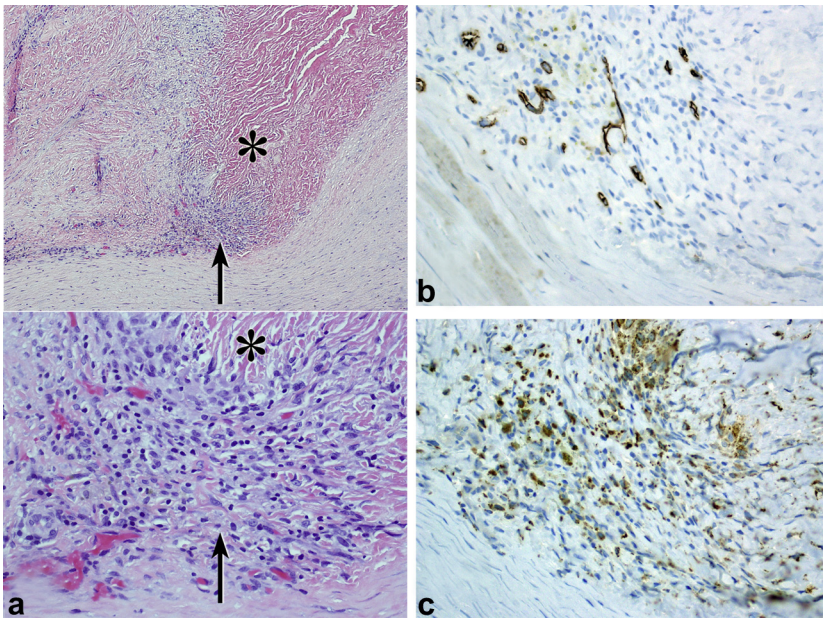

Fig 3. Antibody stains for endothelial cells (P34) and macrophages (P68) in area of SIS patch (mid-portion of Fig 1, *b*). **a,** Low and high power hematoxylin and eosin stain of small intestinal submucosa (SIS) remnant (*) and adjacent cellular infiltrate (*arrow*). **b,** Brown P34 stain shows neovascularization indicating synthetic processes. **c,** P68, which also stains brown, shows macrophage infiltration consistent with ongoing destructive process.

postimplantation in 10% of patients are remarkably similar to those of McCready et al. In contrast, our degenerated patches were implanted over a 14-week period at different hospitals, suggesting the possibility of multiple material lots with unpredictable properties. Additionally, all pseudoaneurysms were repaired using groin SVP without morbidity or mortality.

Although SIS is biologically derived, the Food and Drug Administration classifies it as an intracardiac patch or pledget made of polypropylene, polyethylene terephthalate, or polytetrafluoroethylene. It was approved based on in vitro equivalence to predicate devices. In humans, prosthetic and glutaraldehyde cross-linked bovine pericardial patches maintain their structural integrity while healing as foreign body with characteristic inflammation and scarring. Many pseudoaneurysms result from suture line patch separation because of either technical error or infection. In our series, intact suture lines and negative intraoperative patch cultures indicated no technical or infectious etiology. Histologic findings support the concept that SIS patches undergo breakdown and require ingrowth from surrounding host tissue to maintain integrity. We have traditionally used Dacron patches for carotid closure and performed intraoperative duplex[7] followed by 6- and 12-month surveillance scans. The CorMatrix ECM (CorMatrix Cardiovascular, Inc) was chosen for its handling ease and minimal bleeding at implantation. Although a 6-week scan may allow early detection of pseudoaneurysm degeneration, prevention of such a complication is a better option. In a pressurized arterial environment, especially in the carotid position, biologic patches should be used with caution as imbalances between degradation and host tissue synthesis may unpredictably affect patch integrity.

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Submitted Mar 31, 2013; accepted May 7, 2013.